IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Richard L. Franklin
Application No. 10/750,184
Docket No.: ARC-1001USCON1
For: Removing Dental Plaque With Krill Enzymes

Confirmation No.: 4994
Filing Date: December 31, 2003
Examiner: Zachariah Lucas

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Claims 142-153 and 157-164 stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent no. 4,837,009 (Ractliff), in view of U.S. Patent no. 4,963,491 (Hellgren) and EP 0 257 003 (Karlstam) in the Final Rejection dated March 1, 2010 ("FR").

The Examiner admits that none of the cited references discloses a method for removing dental plaque. See Section 8, page 3 of the FR. Thus, the question is whether it would have been obvious to modify the method disclosed in Ractliff to arrive at the present invention.

Ractliff discloses a method to reduce or prevent plaque formation using chlorine dioxide to oxidize the sulphide bonds in sulphated compounds including glucoseamineglycans (GAGs). Ractliff, however, fails to teach a method for removing already formed dental plaque. Ractliff only indicates how to reduce or prevent formation of plaque. Ractliff also fails to mention enzymes isolated from krill. Thus, to arrive at the present invention starting from Ractliff, a skilled person must: (1) modify the method of Ractliff from a method for reducing or preventing plaque formation to a method for removing plaque, and (2) further modify the method to employ a krill-derived enzyme.

The Examiner disregards many of applicant's arguments on the basis that "one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references." See Section 8, p. 3 of the FR. This is error by the Examiner since the Applicant's arguments, taken together, are a showing that due to deficiencies in the teachings of the references, a skilled person would not make the two modifications to the method of Ractliff to arrive at the invention and would have no expectation of successfully removing plaque based on the teachings of the cited references.

The rejection is based on the Examiner's mistaken perception that Ractliff teaches plaque removal. The Examiner has stated that, "Ratcliff [sic] also teaches a composition (ClO_2) capable of breaking down the matrix components [of a plaque mass] and thereby help in the removal and prevention of dental plaque." Col. 4, ll. 10-23." See p. 8, ll. 2-3 of the

1/17/2008 Office Action. The key point is that the phrase "remove plaque" does not appear in Ractliff, but rather has been added by the Examiner. Ractliff actually teaches that sulphide components of the plaque mass become unstable in the presence of high oxygen compounds (e.g. ClO_2) since the oxygen splits the sulphide bonds to form sulphates. Col. 4, lines 6-9. Thus, in the method of Ractliff, the ClO_2 converts a component of plaque (i.e. sulphides) to another material (i.e. sulphates). This is not a teaching of removing plaque from teeth, but rather is only a teaching that the ClO_2 of Ractliff changes the composition of a component of the plaque. The Examiner, who has the burden of making out a case of *prima facie* obviousness, has not shown that changing the composition of certain sulphide components in plaque to sulphates would result in plaque removal.

Plaque is a complex and dense material mass composed of glucans; fructans; dead cells; cell debris; food debris; high molecular weight polymers; altered salivary glycoproteins, proteases, chemotactic and inflammatory inducing substances; and organisms (See Ractliff, col. 1, ll. 58-68). In view of the complex structure of plaque, there is no reasonable basis for concluding that the composition of Ractliff would necessarily be effective for removing plaque simply because it chemically alters one particular component of the plaque from a sulphide to a sulphate. The Examiner has not provided evidence to substantiate this conclusory assertion.

Furthermore, the change from sulphides to sulphates caused by the ClO_2 of Ractliff may actually be detrimental to plaque removal since Ractliff expressly states that, "[n]o disulphate enzymes capable of cleaning the sulphate moieties of glycoproteins are known" (col. 3, lines 59-61). Thus, the creation of such suphate moieties using the method of Ractliff may make it harder to remove plaque. Thus, Ractliff does not disclose a method for plaque removal.

Hellgren teaches a cleaning method using krill derived enzymes. Hellgren mentions that the cleaning method can be used to clean teeth. (col. 1, line 31). The Examiner admits that Hellgren does not mention removal of dental plaque (See p.8, ll. 15-16 of the 1/17/2008 Office Action). Rather, the Examiner relies on the teaching of Hellgren that krill-derived enzymes can be used to remove biological contaminants from teeth. The problem with this is that Hellgren only indicates that the biological contaminants fibrin, blood crusts, coagulated blood, pus and necrotic tissue are removed by krill enzymes. Col. 4, ll. 19-22. The Examiner has not demonstrated that any of these biological contaminants are present in dental plaque.

Although Hellgren contains a broad disclosure that krill-derived enzymes are useful to

remove contaminants containing mixtures of lipids, phospholipids, biopolymers such as proteins, peptides, nucleic acids, mucopolysaccharides, polysaccharides and degradation products thereof (col. 3, ll. 31-37 of Hellgren), the examiner has presented no evidence that shows that the specific materials contained in dental plaque would, in fact, be removed by krill-derived enzymes. Hellgren does not indicate that all such materials are removed by krill-enzymes, but only that the krill-derived enzymes may be useful if a contaminant contains such materials. Hellgren only identifies fibrin, blood crusts, coagulated blood, pus and necrotic tissue as contaminants which can be removed by krill-derived enzymes but has not mentioned dental plaque.

An important point in relation to Hellgren is that even assuming that the krill-derived enzymes of Hellgren may degrade certain components of plaque (which has not been demonstrated by the Examiner), this alone may not be sufficient to remove plaque. Rather, a mere chemical change by degradation of one material to another may not be sufficient to remove the dense mass that forms plaque from the teeth. In fact, the Examiner has not provided a teaching that degradation of one or more components of plaque is sufficient to achieve plaque removal. Further, the degraded components might be a small proportion of the overall plaque mass and thus degradation of these components, taken alone, might not be sufficient to remove the plaque. Also, there is no showing by the Examiner that even if plaque components are degraded by krill-derived enzymes, that these components are critical to plaque adhesion and thus their degradation would result in plaque removal.

To sum up, the Examiner has not demonstrated that the prior art teaches that: (1) krill-derived enzymes actually degrade components of plaque, (2) that degradation of certain components of plaque results in plaque removal, and (3) that even if some plaque components were degraded by krill-derived enzymes, that these components are present in sufficient quantity in the plaque and play a role in plaque adhesion such that their degradation would result in plaque removal. Thus, Hellgren does not give sufficient information for a skilled person to conclude that dental plaque would be removed from teeth using krill-derived enzymes. Therefore, since Hellgren does not teach or suggest a method for removing dental plaque, and does not give sufficient information to conclude that krill-derived enzymes would remove dental plaque, Hellgren would not motivate a skilled person to modify the method of Ractliff to a method for removing dental plaque.

The Examiner has also conceded that Karlstam does not teach the use of a krill-derived enzyme to degrade plaque (p. 8, last two lines of the 1/17/2008 Office Action). Thus, there is no reference among the three references relied on in the rejection which teaches a method for removing plaque. Accordingly, there is no basis for a skilled person to modify the method of Ractliff from a method of preventing or reducing plaque formation to a method for removing dental plaque. The rejection should be withdrawn for this reason alone.

With respect to modification (2) to the method of Ractliff, none of the references of record teach that the krill-derived enzymes, as claimed, would be effective to remove dental plaque. The Examiner has admitted that Hellgren does not teach a method for removing dental plaque. Further, for the reasons given above, there is insufficient information in Hellgren for a skilled person to conclude that krill-derived enzymes would be effective for removing dental plaque.

The Examiner concludes that Karlstam teaches that krill derived enzymes degrade glycosoaminoglycans (GAGs) but this is incorrect (p. 2, ll. 14-15 of Advisory Action of 11/26/2008). Karlstam, actually teaches that Antarctic krill contains hyaluronidase which cleaves the glucoronic acid linkages of hyaluronic acid (p. 2, ll. 29-32; page 3, ll. 5-6). The Examiner's reliance on p. 2, ll. 18-22 of Karlstam as teaching that krill-derived enzymes degrade all GAG's in incorrect as this passage of Karlstam does not state this.

The Examiner connects Karlstam to Ractliff on the basis that Ractliff indicates that the plaque mass may contain sulphated GAGs (col. 3, ll. 65-67). However, a skilled person would not conclude that the hyaluronidase of Karlstam would be effective on plaque since Ractliff does not indicate that plaque contains hyaluronic acid, the specific material which is degraded by the hyaluronidase of Karlstam. Further, hyaluronic acid is not a sulphated GAG and thus does not even fit within the class of plaque materials referenced in Ractliff. Thus, since the Examiner has not demonstrated that hyaluronic acid is a component of plaque and because hyaluronic acid is not a sulphated GAG, a skilled person would not conclude that the hyaluronidase of Karlstam would degrade plaque or be useful for plaque removal. As a result, the Examiner's basis for using the hyaluronidase of Karlstam for plaque removal is incorrect, as is the Examiner's basis for an expectation of successful plaque removal using the hyaluronidase of Karlstam.

Alternatively, the Examiner asserts that Ractliff inherently discloses a method for

removing plaque by virtue of the repeated application of the chlorine dioxide compounds to retard plaque growth. This conclusion is incorrect and not supported by evidence. As discussed above, the only activity Ractliff discloses for chlorine dioxide in relation to the plaque mass is to convert sulphated compounds to sulphates. The Examiner has not shown that this conversion would inherently result in plaque removal since there is no evidence that: (1) the sulphated compounds form a significant proportion of the plaque mass, and (2) the sulphated compounds play a role in plaque adhesion. "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference... Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir.1999). The Examiner has not met the burden of showing that repeated chlorine dioxide treatments in accordance with Racliff necessarily remove plaque.

Ractliff teaches that ClO_2 oxidizes sulphide bonds of sulphated GAGs. Neither Karlstam nor Hellgren teaches that krill-derived enzymes are capable of oxidizing sulphide bonds of sulphated GAGs. Thus, a skilled person would not substitute krill-derived enzymes for the ClO_2 of Ractliff since there is no evidence that the krill-derived enzymes would achieve the desired oxidation reaction of the ClO_2 of Ractliff. Rather, the mechanism of action of the krill enzymes of Karlstam and Hellgren is completely different than the mechanism of action described in Ractliff and thus there is no motivation to combine the references. Further, even assuming that such a combination were made, there is no basis for an expectation that such a combination would effectively remove dental plaque as discussed above.

Withdrawal of the rejection and issuance of a Notice of Allowance are requested.

Respectfully submitted,

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